Journal of Psychiatric Research 47 (2013) 91–104

Contents lists available at SciVerse ScienceDirect

Journal of Psychiatric Research

journal homepage: www.elsevier.com/locate/psychires

Review

Executive functions rehabilitation for schizophrenia: A critical systematic review

B. Kluwe-Schiavon [a,*], B. Sanvicente-Vieira [a], C.H. Kristensen [a], R. Grassi-Oliveira [a,b]

[a] Centre of Studies and Research in Traumatic Stress, Pontifical Catholic University of Rio Grande do Sul, Brazil
[b] Biomedical Research Institute, Centre of Studies and Research in Traumatic Stress, Pontifical Catholic University of Rio Grande do Sul, Brazil

ARTICLE INFO

Article history:
Received 10 September 2012
Received in revised form
30 September 2012
Accepted 2 October 2012

Keywords:
Rehabilitation
Executive functions
Working memory
Neuropsychology
Psychotherapy
Schizophrenia

ABSTRACT

Background: Consistent evidences suggest that poor functional outcomes in schizophrenia are associated with deficits in executive functions (EF). As result cognitive training, remediation and/or rehabilitation (CR) programs have been developed and many theories, methods and approaches have emerged in support of them. This article presents a systematic review of randomized controlled trials (RCT), including EF rehabilitation interventions, with a focus on methodological issues and evidences of EF improvements.

Method: Eletronic databases (Medline, Web of Science, PsycINFO and Embase) were searched for articles on schizophrenia, EF and cognitive rehabilitation terms. The methodological quality of each article was measured by 5-point JADAD scale.

Results: A total of 184 articles were initially identified, but after exclusion criteria, 30 RCT remained in this review. A proportion of 23% of studies scored higher than 4 points in JADAD scale, 40% scored 3 points, 33% scored 2 points and one study scored only 1 point. The average length of interventions was approximately 80 h distributed around 3.42 h/week.

Conclusion: The reviewed articles corroborate the literature pointing that CR could be a promising therapeutic option for cognitive deficits in schizophrenia. In general, CR could improve cognitive domains and social adjustment either using computerized or paper-and-pencil programs. Additionally, CR combined with cognitive behavioral therapy and/or group sessions is particularly effective. In this paper, we also speculated and discussed optimal doses of treatment and the differences regarding modalities and approaches.

For at least five decades the chronic nature of schizophrenia has been recognized and considerable research and clinical attention have been paid to the cognitive impairments in schizophrenia (Goff et al., 2011; Harrison, 1995). Consistent evidence suggests that poor functional outcomes – in social ability, vocational adjustment, quality of life or even symptom severity – are associated with deficits in psychomotor speed, attention, information processing, memory and particularly executive functions (EF) (Bell et al., 2009; Kurtz et al., 2001; Penades et al., 2003; Velligan et al., 2006; Wykes and Spaulding, 2011).

EF deficits are thought to be a key barrier to functioning in schizophrenia, with some authors suggesting that schizophrenia is primarily a frontostriatal disorder and that executive cognitive deficits progress during the course of the disease (Hutton et al., 1998; Krieger et al., 2005; Liu et al., 2011). Consistent evidence had pointed that patients with schizophrenia showed reduced activation in the left dorsolateral prefrontal cortex, rostral/dorsal anterior cingulate cortex, left thalamus, and inferior/posterior cortical areas; consistently associated with impaired EF (Minzenberg et al., 2009). Therefore, cognitive enhancement interventions programs have been achieving importance and interest because they may provide direct benefits to patients with executive dysfunctions (Reeder et al., 2004; Wykes et al., 2011; Wykes et al., 1999).

Many efforts were done in this direction, but some discrepancies between studies still are a problem for the field, including define an accurate terminology to identify such interventions. Notwithstanding, "remediation" implies a curative treatment and compensatory strategies while "rehabilitation" implies a restoration of premorbid levels (Twamley et al., 2003). Considering the chronicity of schizophrenia disorder and the issues about premorbid functioning the accuracy in using terms as "remediation" or "rehabilitation" still an open discussion. Therefore the term "training" may be preferable, since it represents "an organized system of education, instruction, or discipline" (Fisher et al., 2010; Twamley et al., 2003; Vinogradov et al., 2009). In this review we considered cognitive rehabilitation, remediation and/or training (CR) as a set of cognitive enhancing interventions. During the past few years, many

* Corresponding author.
E-mail address: brunokluwe@gmail.com (B. Kluwe-Schiavon).

0022-3956/$ – see front matter © 2012 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.jpsychires.2012.10.001

different CR programs, including EF rehabilitation, have been developed, and as a result, many theories, methods and approaches have emerged in support of CR. Different CR programs usually differ in administration, typically utilizing either computer-based (computerized) or paper-and-pencil (non-computerized) tasks. The main approaches generally address: (a) functional adaptation (daily life activities), (b) general stimulation (non-specific training that must involve multiple cognitive abilities), and/or (c) process-specific approaches (that directly strengthen the requisite cognitive skills).

Moreover, CR understanding should be based on concepts of the therapeutic milieu developed by Ben-Yishay (1996) and those already widely used in brain injury programs, development of skills is observed as part of a larger process which must involve psychoeducation, social adjustment and vocational reorganization (BenYishay, 1996). Neurocognitive impairments may have an adverse effect on social cognition and thereby exert a negative influence on functional status (Schmidt et al., 2011). Specifically improvement in EF predicted improvement in daily functioning among persons with chronic schizophrenia who had current negative symptoms and evidenced neuropsychological impairments (Penades et al., 2010). The authors also found that after CR intervention improvements in cognitive functions that were not significantly associated with daily functioning at baseline led to improve daily functioning. The authors concluded that even if persons have impairments in multiple cognitive domains executive functioning still needs to be the target of the intervention (Penades et al., 2010).

Despite the potential importance of CR, there are only a few meta-analyses, showing small to moderate effects of CR on cognitive outcomes at post-treatment and follow-up assessments in individuals with schizophrenia diagnosis (McGurk et al., 2007b; Wykes et al., 2011) and none specifically reviewing EF rehabilitation.

1. Aims of the study

Considering (1) the importance of executive deficits in the chronic nature of schizophrenia and the considerable interest in executive rehabilitation to reduce cognitive deficits and benefit to patient functioning and (2) the relative heterogeneity of CR programs, including executive rehabilitation, this article presents a systematic review of CR randomized controlled trials (RCT) including EF rehabilitation interventions, with a focus on methodological issues and evidences of EF improvements.

2. Methods

Following the recommendation checklist of Cochrane in how to develop a search strategy (CHMG, 2007), the search was performed in Medline, Web of Science, PsycINFO and Embase databases. The searched terms were [“executive functions OR executive function OR processing speed OR speed processing OR working memory”] AND [“schizophrenia”] AND [“cognitive rehabilitation” OR “cognitive remediation OR cognitive training OR cognitive enhancement OR neurocognitive enhancement”]. The limits were “English-language articles”, “randomized control trials”, “humans”, and “published since 2001.” The search criteria were the presence of key terms in the title/abstract or topic. The exclusion criteria were: non-English articles, no rehabilitation as part of the intervention, no EF outcomes as dependent measures, republished data, non-randomized controlled trial articles and trials with no schizophrenia or schizoaffective disorder participants. Initially, two investigators (BKS and BSV) independently screened the titles and abstracts of potentially relevant studies for eligibility. When the information was not sufficient to determine if the article was eligible for inclusion, the article’s full text was obtained for further evaluation. Discrepancies were discussed until consensus was reached. The same procedure was done regarding review of the eligible studies. The authors also screened the reference list of each included paper for additional studies not recovered in the database search.

The methodological quality of each article was measured by its JADAD score on a 5-point scale (Jadad et al., 1996). In the first step, the JADAD scale consists of a three-point questionnaire in which each question is answered with either a yes (one point) or a no (zero points). The three-point questionnaire investigates whether the articles are (1) randomized, (2) double blind, and (3) if there are descriptions of study withdrawals and dropouts. In a second step, additional points are given (4) if the method of randomization is appropriate and (5) if the method of blinding is appropriate. Points are either given if methods are appropriate or subtracted if they are not.

3. Results

The search identified 184 papers that were then screened by hand and submitted to the exclusion criteria. The flowchart is shown in Fig. 1. Although there were 33 resulting individual articles, six studies are follow-up assessments of previous RCT (ID 2, 9 and 11 in Table 1) and then regrouped according with it (Cavallaro et al., 2009; Fisher et al., 2009, 2010; Hogarty et al., 2004, 2006; Poletti et al., 2010).

3.1. Methodological quality

Table 1 provides an overview of the methodological quality of the 30 included RCT and their primary characteristics: sample and measures. All studies were analyzed according with JADAD scale. Seven studies (23%) were scored as higher methodological quality (5 points) but one of them did not control for psychopharmacological treatment. Six studies (40%) were initially given 4 points according to JADAD raw criteria in the first step, including one study that did not control for psychopharmacological treatment effects. However, considering that all six were single-blind studies, one point was then subtracted according with JADAD criteria due “inadequate method of masking,” resulting in a final score of 3 points for all of them. Ten studies (33%) scored 2 on the JADAD scale because they were not blinded, including three studies that did not control for psychopharmacological treatment. One study scored 1 point for the quality of method.

3.2. Studies design

In general, studies used baseline assessments with clinical, neuropsychological and quality of life measures. After this procedure, the participants were randomly assigned to an intervention type. Follow-up assessments were often applied at the end of the initial intervention time and, in some studies, after an additional waiting period. Table 2 provides an overview of each CR program (frequency per week and total hours) and the individual methodological implementations, which are shown descriptively in Table 3. The average length of interventions was approximately 80 h distributed around 3.42 h/week.

3.3. Longitudinal dimension

Fig. 2 illustrates total intervention times (weeks) and all assessments during the follow-up. Eleven studies (36%) included a waiting time – the time between the end of the intervention and the final assessment – in their design that ranged from 1 month to 12 months after the intervention. Most studies included assessments only at the pre-test and post-test. Total intervention time was, on average,

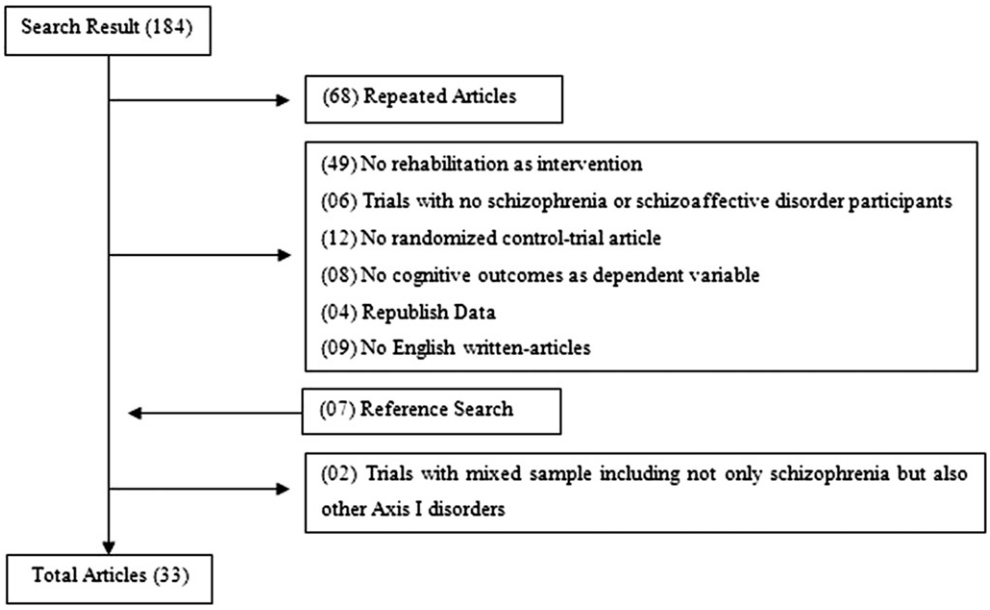

Fig. 1. Flowchart of systematic review.

23 weeks, although programs varied from 3 weeks (Rodewald et al., 2011; Sartory et al., 2005) to 48 weeks (Cavallaro et al., 2009; Greig et al., 2007; Kurtz et al., 2007).

3.4. Assessments

3.4.1. Neuropsychological

Table 1 also describes neuropsychological and clinical assessments and the tests or tasks utilized. Neuropsychological measures investigated in the studies were typically categorized into six cognitive domains: IQ, Attention, Working Memory, Memory, Processing Speed and EF. Only five studies (26%) controlled baseline IQ. Eleven studies (36%) assessed attention. Working memory was formally assessed in seventeen studies (56%), and memory processes were assessed in 20 (66%) studies, including eight different memory skills (visual learning memory, verbal learning memory, episodic memory, verbal memory, immediate verbal memory, visual episodic and visual special episodic memory and nonverbal memory).

All articles measured EF explicitly ($n = 18$) or non explicitly ($n = 12$) (i.e., when authors did not explicitly stated that EF was being assessed). Five studies assessed Planning/Reasoning and Problem Solving, which we considered EF domains and included among the non-explicit measurements. Seven studies had wide-ranging cognitive constructs, and their specific EF measures were assessed by considering the tasks used. Eight studies made a distinction between processing speed and EF, although the tasks used to measure processing speed did not always adequately distinguish themselves from the tasks used to measure EF. There was an average of three tasks per study and approximately 30 different tasks were employed to assess different EF constructs. The most commonly used test was the Wisconsin Card Sorting Test (WCST), and the second one the Trail Making Test – Part B (TMTB). However, TMTB was also considered a measure of attention, working memory and processing speed. An average of two tasks per study were used to assess processing speed, and the most commonly used tasks were the Stroop Color Interference Test and the Trail Making Test – Part A (TMTA). There was no homogeneity, or even agreement, between studies regarding specific EF tasks and their corresponding cognitive domains.

3.4.2. Clinical

Twenty-three studies (76%) assessed both positive and negative symptoms of schizophrenia. Seventeen studies had pre-test and pos-test measures, six had only a pre-test, and seven did not control this variable. The Positive and Negative Syndrome Scale (PANSS) was the most frequently used instrument, adopted by twelve studies. The Brief Psychiatric Rating Scale (BPRS) and the Scale for the Assessment of Negative Symptoms (SANS) were also commonly used.

3.4.3. Social adjustment and quality of life

Social Adjustment and Quality of Life were measured by sixteen studies (52%), as we considered all functional assessments mentioned by the authors (including social inference, affect recognition, social cognition, social knowledge, facial affect recognition, everyday community functioning) (Table 1). The average number of instruments used to assess these domains was 2.25; however, one study alone utilized seven tests, given that its aim was to examine the effects of Cognitive Enhancement Therapy (CET) on cognitive and functional outcomes in early-course schizophrenia (Eack et al., 2009).

3.5. Interventions

3.5.1. CR outcomes

CR programs may differ in their epistemological bases, their goals and techniques, or even their methods. In our results, we categorize the programs by their different administered procedures as follows: computer-based, paper-and-pencil, or vocational. As CR programs also differ by theoretical approaches, including process-specific, general stimulation or functional adaptation, the results are presented as combinations of these approaches according to their designs. The outcomes from the CR programs are presented in Table 4.

3.5.2. Computer-based programs

When compared with waiting list conditions, computer-based cognitive remediation therapy was generally effective in improving performance on attention, memory, logic thought, reasoning and EF tasks (d'Amato et al., 2011); however, one study did not find a group

Table 1
Methodological quality and characteristics of the studies.

ID	JADAD	Author (Year)	Total sample [age, mean (SD)]	Measures
1	5a	(Bell et al., 2001)	145 participants with schizophrenia or schizoaffective disorder [42.75 (9)]	Affect Recognition: BLERT Attention: CPT Executive Functions: WCST; GPT Intelligence: DSS-WAIS; VR-WAIS; FM-WAIS; LM-WMS Memory: HVLT Social Inference: Hinting Test Symptoms: PANSS Working Memory: BLERT; DS-WAIS; LNS-WAIS; TMTB
2	5a	(Fisher et al., 2010)[b] (Fisher et al., 2009)[b]	32 patients with schizophrenia disorder [46.1 (8.05)] 55 outpatients with schizophrenia disorder [44.08 (9.73)]	Attention: CPT; Cognitive Control: TOL; TMTB Nonverbal Working Memory: Spatial Span, Visual Learning Speed of Processing: SC-MATRICS; TMTA; Category Fluency Animal Training Verbal Learning and Memory: HVLT Visual Learning and Memory: BVMT Problem Solving: TOL Social Cognition: MSCEIT Quality of Life: QLS Symptoms: PANSS
3	5a	(Medalia et al., 2001)	54 patients with schizophrenia ($n = 41$) and schizoaffective ($n = 13$) disorder [36.33 (7.33)]	Neuropsychological Measures: C-WAIS; LM-WMS; ILS-PS
4	5a	(Ojeda et al., 2012)	76 patients with schizophrenia disorder [35.78 (9)]	Processing Speed: Stroop; Grooved Pegboard Verbal Fluency: Barcelona Verbal Fluency Subtest Learning and Memory: HVLT Executive Function: TMTB Attention: DS-WAIS; Symbol Search; TMTA Working Memory: DS-WAIS; DS-WAIS Functional Evaluation: DAS-WHO Symptoms: PANSS; SAI
5	5a	(Penades et al., 2006)	40 patients with schizophrenia disorder [36.16(8.63)]	Estimated IQ: V-WAIS Executive Functions: WCST; Stroop; TMTB; ILS-PS Nonverbal Memory: VR-WMS; F-WMS Psychomotor Speed: DSC-WAIS; TMTA Symptoms: PANSS Verbal Memory: RAVLT; LM-WMS Working Memory: DS-WAIS; LNS-WAIS; A-WAIS
6	5a	(van der Gaag et al., 2002)	42 in patients with schizophrenia disorder [31.05 (8.0)]	Attention: CPT; SAT; Tem-Letter Array; TMTA; TMTB; Stroop Executive Function: WCST; Word Fluency; PA-WAIS Memory: RAVLT; Rey-CFT; DSS-WAIS Perception: Emotion Matching Test; Emotion Labeling Test
7	5b	(d'Amato et al., 2011)	77 patients with schizophrenia disorder [32.8 (6.45)]	Attention: CPT; Nonverbal Working Memory: SWMT Quality of Life: SQOL; EAS Reasoning and Problem Solving: STDT; WCST Speed of Processing: Finger Topping Test Symptoms: PANSS Verbal Learning and Memory: WLMT Verbal Working Memory: ANS Visual Learning and Memory: Face Memory Test
8	3a	(Cavallaro et al., 2009)[a] (Poletti et al., 2010)[a]	100 patients with schizophrenia disorder [33.7 (8.15)]	Neuropsychological Assessment: VM-BACS; WM-BACS; PC-BACS; LF-BACS; SF-BACS; SC-BACS; P-BACS; WCST; CPT Quality of Life: QLS Symptoms: PANSS
9	3a	(Hodge et al., 2010)	69 patients with schizophrenia, schizophreniform, schizoaffective disorder [31.33 (9.08)]	Cognitive Function: TMTA; TMTB; CPT; RAVLT; Rey-CFT; Delis-Kaplan Executive Function System Psychosocial Function: Social and Occupational Function Scale; LSP; WHOQOL; Symptoms: The Rosenberg Self Steem Scale; PANSS; Calgary Depression Scale;
10	3a	(Hogarty et al., 2004)[a] (Hogarty et al., 2006)[a]	121 patients with schizophrenia or schizoaffective disorder [37.3 (8.9)]	Cognitive flexibility/problem solving: TMTB; PA-WAIS; WCST Psychomotor Speed: DSS-WAIS Verbal Memory: VM-WMS; CVLT Working Memory: DS-WAIS Language: V-WAIS Social adjustment: Major Role Adjustment Inventory; GAS; Social Security (employability) Criteria Symptoms: BPRS; WNSS; Raskin Depression Scale; Patient Subjective Responses Questionnaire
11	3a	(Kurtz et al., 2007)	33 participants [34.8 (10.75)]	Executive Function: BD-WAIS; Rey-CFT; BCT; Penn-CET Speed of Information Processing: DS-WAIS; SS-WAIS; GPT; TMTA; TMTB; LF-BACS Verbal Episodic Memory: LM-WMS; CVLT Visual Spatial Episodic Memory: Rey-CFT Working Memory: DS-WAIS; A-WAIS; LNS-WAIS
12	3a	(Rodewald et al., 2011)	89 inpatients with schizophrenia disorder [28.74 (7.23)]	Functional Capacity: O-AFP IQ: MWT-B Planning and Problem-Solving: TOL; Zoo Map; PPSS-Plan-a-Day

Table 1 (*continued*)

ID	JADAD	Author (Year)	Total sample [age, mean (SD)]	Measures
				Processing Speed: TMTA; TMTB; Stroop Symptoms: PANSS Task Motivation: FEAM Working Memory: DS-WAIS; LNS-WAIS; Corsi BTT
13	3a	(Ruiz et al., 2011)	22 patients with schizophrenia disorder [38.77 (8.84)]	Executive Functions: WCST Working Memory: DS-WAIS; A-WAIS Psychomotor Speed: DSS-WAIS Attention: PA-WAIS Memory: RBMT Symptoms: BPRS; LSP
14	3a	(Vinogradov et al., 2009)	55 schizophrenia outpatients [43.86 (10.29)]	Nonverbal Working Memory: MATRICS Problem Solving: MATRICS Speed of Processing: MATRICS Verbal Learning and Memory: MATRICS Verbal Working Memory: MATRICS Visual Learning and Memory: MATRICS Global Cognition: MATRICS Symptoms: PANSS
15	3a	(Vita et al., 2011)	32 patients schizophrenia with disorder [37.25 (8.1)]	Attention: TMTA Executive Functions: TMTB; TMTB; WCST Memory: CVLT Psychosocial Functioning: Personal Social Functioning Scale Working Memory: Self-Order Pointing Task; Visual Conditional Associative Learning Task Symptoms: PANSS; Health of the Nation Outcome Scale
16	3a	(Antonio Vita et al., 2011)	84 patients with schizophrenia disorder [39 (9.9)]	Processing Speed: TMTA Working Memory:, TMTB; Self-Order Pointing Task Verbal Memory: CVLT Executive Functions: TMTA; TMTB; WCST; Self-Order Pointing Task Psychosocial Functioning: GAF; Health of the Nation Outcome Scale Symptoms: PANSS
17	3a	(Wykes et al., 2007a)	40 adolescent patients with schizophrenia disorder [18.2 (2.5)]	Cognitive flexibility: WCST Memory: DS-WAIS Planning: Modified Six Elements Test Secondary outcomes: Social Behaviors Schedule; BPRS; QLS; Rosenberg Self-Esteem Scale
18	3a	(Wykes et al., 2007b)	85 schizophrenia patients with cognitive and social problems [36 (−)]	Flexibility: WCST Planning: BADS Symptoms: PANSS, Social Behavior Schedule Working Memory: DS-WAIS
19	3b	(Katz and Keren, 2011)	37 clients [30 (8.83)]	Executive Functions: WCST; DS-WAIS; BADS; EFPT Symptoms: PANSS
20	2a	(Bell et al., 2007)	53 [41.9 (9.9)] 63 [43.6 (8.1)]	Attention: CPT Memory: HVLT; FM-WMS Neuropsychological Measures: Digit Symbol Substitution-WMS; Digit Span-WMS; LNS-WMS; VR-WMS; LM-WMS; HVLT; Hopkins; Hinting Test; TMTB Executive Function: WCST; GPT Affect Recognition: BLERT
21	2a	(Dickinson et al., 2010)	69 outpatients [47.7 (7.7)]	Attention: Stroop; CPT Episodic memory: HVLT; RBANS-SM; BVMT Executive Functioning: BACS; DKEFS; TQT; TMTB Everyday Community Functioning: MASC; UCSD Processing speed: Digit Symbol Coding MATRICS; DKEFS; TMTA; Stroop; ECF; Symptoms: BPRS; SANS Working Memory: N-Back; LNS-WAIS
22	2a	(Eack et al., 2009)	58 early outpatients with schizophrenia ($n = 38$) and schizoaffective ($n = 20$) disorder [25.92 (6.36)]	Cognitive Style: CSI Executive Functions: TMTB; PA-WAIS; WCST; TOL Language: V-WAIS Neurological Soft Signs: Neurological Evaluation Scale Psychomotor Speed: DSS-WAIS Social Adjustment: SAS-II; GAS; MRI; PPI Social Cognition: SCP; MSCEIT; CSSC Interview Symptoms BPRS; WNSS; RDS; CAS; PSR Questionnaire Verbal Memory: CVLT Working Memory: DS-WAIS
23	2a	(Lopez-Luengo and Vazquez, 2003)	24 outpatients [33.45 (8.65)]	Attention: CPT; CT; Dichotic-Listening Task; Dual Task; TMTA; TMTB; PASAT; EAQ Executive Functions: WCST Memory: CVLT Symptoms BPRS; SANS; GAF
24	2a	(Matsui et al., 2009)	20 patients with schizophrenia disorder [32.7 (6.9)]	Executive Function: RSCT; JT; Zoo Map; BST Social Knowledge: Script Test Verbal Memory: JSMT; DS-WAIS Symptoms: SAPS; SANS
25	2a	(Royer et al., 2012)		

(*continued on next page*)

Table 1 (*continued*)

ID	JADAD	Author (Year)	Total sample [age, mean (SD)]	Measures
			59 patients with schizophrenia disorder [33.25 (8.3)]	Attention: Computerized Battery Inhibition: Go-no-Go; Hayling; Stroop Working Memory: DS-WAIS; N-Back Long-Term Memory: Grober and Buschke Test Executive Function: Verbal Fluency Test; WCST Planning: Ecological Shopping Test IQ: WAIS
26	2a	(Wölwer et al., 2005)	77 patients with schizophrenia disorder [34.46 (9.8)]	Attention: D2; TMTA Executive Functions: Five Point Test; FAS; TMTB; Facial Affect Recognition: Pictures of Facial Affect; Benton FRT Memory: DS-WAIS; AVLT Situational Understanding: PA-WAIS Symptoms: PANSS
27	2b	(Greig et al., 2007)	72 outpatients with schizophrenia ($n = 21$) and schizoaffective disorder ($n = 51$) [40.11 (9.27)]	Executive Function: WCST Visual and Verbal Memory: LM-WMS; VR-WMS; HVLT Social Cognition: Hinting Test; BLERT Symptoms: PANSS Working Memory: DS-WAIS; LNS-WAIS
28	2b	(Bio, Gattaz, 2011)	112 outpatients with schizophrenia disorder [29.5 (7.4)]	Neuropsychological Measures: DS-WAIS; C-WAIS; Stroop Symptoms: PANSS
29	2b	(Sartory et al., 2005)	42 inpatients with schizophrenia disorder [31.9 (8.7)]	Executive Functions: TMTB; DSS-WAIS; LM-WMS Estimate IQ: Multiple Word Recognition Test Word fluency: S, G, U, N, F, T, J, P,/1 min each;
30	1a	(Fiszdon et al., 2004)	152 outpatients with schizophrenia or schizoaffective disorder [42.55 (8.95)]	Cognitive Function: DS-WAIS, Words sequenced recall CogRehab Software; IQ: WAIS Symptoms: PANSS

Note 1: A-WAIS: Arithmetic, WAIS; ANS: Auditory Number Sequencing; AS-BACS: Selective Attention; AVLT: Auditory Verbal Learning Test; BACS: Brief Assessment of Cognition in Schizophrenia; BADS: Behavioral Assessment of the Dysexecutive Syndrome; Benton FRT: Benton Face Recognition Test; BCT: Booklet Category Test; BD-WAIS: Block design, WAIS; Benton FRT: Benton Face Recognition Test; BLERT: Bell Lysaker Emotion Recognition Task; BPRS: Symptoms Brief Psychiatric Rating Scale; BST: Ball Search Test; BVMT: Brief Visuospatial Memory Test; CAS: Covi Anxiety Scale; Corsi BTT: Corsi Block Taping Task; CPT: Continuous Perfomance Test; CSI: Cognitive Style Inventory; CSSC Interview: Cognitive Style and Social Cognition Eligibility Interview; CT: Cancellation Task; CVLT: California Verbal Learning Test; C-WAIS: Comprehension, WAIS; D2: Attention Concentration-Endurance-Test D2; DAS-WHO: Disability Assessment Schedule; DKEFS: Delis-Kaplan Executive Functioning System; DSC-WAIS: Digit Symbol Coding, WAIS; DSS-WAIS: Digit Symbol Substitution, WAIS; DS-WAIS: Digit Span, WAIS; EAQ: Everyday Attention Questionnaire; EAS: Social Autonomy Scale; ECF: Everyday Community Functioning; EFPT: Executive Functions Performance Test; FAT: Facial Affect Recognition Pictures – Facial Affect-Test; FAS: FAS Oral; FEAM: Fragebogen zur Erfassung aktueller Motivation; FM-WAIS: Figural Memory, WAIS; FM-WMS: Figural Memory, WMS; F-WMS: Faces I and II, WMS-III; GAF: Global Assessment of Functioning; GAS: Global assessment Scale; GPT: Gorham's Proverbs Test; HVLT: Hopkins Verbal Learning Test; ILS-PS: Independent Living Scale – Problem Solving; JSMT: Japanese Sentence Memory Test; JT: Judgment Test; LF-BACS: Letter Fluency, BACS; LM-WMS: Logical Memory I and II, WMS; LSP: Life Skill Profile; LNS-WAIS: Letter Number Sequencing, WAIS; MATRICS: Measurement and Treatment Research to Improve Cognition in Schizophrenia; MASC: Maryland Assessment of Social Competence; MSCEIT: Mayer-Salovey-Caruso Emotional Intelligence Test; MRI: Major Role inventory; MWT-B: Mehrfachwahl-Wortschatz-Intelligenztest; O-AFP: Osnabruck Work Capabilities Profile; PANSS: Positive and Negative Syndrome Scale; PASAT: Paced Auditory Serial Addition Task; PA-WAIS: Picture Arrangement, WAIS; PCET: Penn Conditional Exclusion Test; P-BACS: Planning, BACS; PC-BACS: Psychomotor Coordination, BACS; Penn-CET: Penn Conditional Exclusion Test; PPI: Performance Potential Inventory; PPSS-Plan-a-Day: Planning and Problem Solving Scenarios, Plan-a-Day; PSR Questionnaire: Patient Subjective Responsive Questionnaire; QLS: Quality of Life Questionnaire; RAVLT: Rey Auditory Verbal Learning Test; RBANS-SM: Repeatable Battery for the Assessment of Neuropsychological Status – Story Memory; RBMT: River mead Behavioral Memory Test; RDS: Raskin Depression Scale; Rey-CFT: Rey Complex Figure Test; RSCT: Rule Shift Cards Test; SAI: Schedule for the Assessment of Insight; SANS: Scale for the Assessment of Negative Symptoms; SAPS: Scale for the Assessment of Positive Symptoms; SAS-II: Social adjustment scale II; SAT: Span of apprehension test; SC-BACS: Symbol Coding; SCP: Social Cognition Profile; SCVLT: Spain-Complutense Verbal Learning Test; SF-BACS: Semantic Fluency, BACS; SC-MATRICS: Symbol Coding MATRICS; SQOL: Self-Report Quality of Life for People with Schizophrenia; Stroop: Stroop Color Word Test; SS-WAIS: Symbol Search, WAIS; STDT: Strategic Target Detection Test; SWMT: Spatial Working Memory Test; TMTA: Trail-Making Test–A; TMTB: Trail-Making Test–B; TOL: Tower of London; TQT: Twenty Questions Task; UCSD: Performance-based Skills Assessment; VM-BACS: Verbal Memory, BACS; VM-WMS: Verbal Memory WMS; VPS: Visual Processing Scanning; VR-WAIS: Visual Reproduction I and II, WAIS; VR-WMS : Visual Reproduction I and II, WMS; V-WAIS: Vocabulary, WAIS; WCST: Wisconsin Card Sorting Test; WMS: Wechsler Memory Scale; WLMT: Word List Memory Test; WM-BACS: Working Memory, BACS; WNSS: Wing Negative Symptoms Scales; WHOQOL: The World Health Organization Quality of Life Scale.
a: Psychopharmacological control; b: No psychopharmacological control.
[a] Follow-up study.
[b] Follow-up study with different samples.

effect favoring computerized interventions (Hodge et al., 2010). The results favoring computerized treatment were also found when the comparison was made with treatment as the baseline condition, in autonomy, memory, word fluency and comprehension (Medalia et al., 2001; Sartory et al., 2005), in addition, two studies found improvement in quality of life measure (Vita et al., 2011b). When compared with a placebo condition (non-domain-specific game activities with low cognitive demand), there was evidence of benefit for CR group in performance either on verbal learning and on global cognition measure (Vinogradov et al., 2009) that was successfully replicated in one study (Fisher et al., 2010) but failed in other one (Dickinson et al., 2010).

General computer stimulation approaches, when compared with computer process-specific approaches, engendered significant improvements in autonomy (Medalia et al., 2001) and solution time in planning and problem-solving training (Rodewald et al., 2011). Even though general cognitive functioning and functional capacity appeared to have improved in both conditions (Rodewald et al., 2011). Similarly, Kurtz and colleagues questioned the mechanism of the treatment effects of the process-specific approaches and their emphasis on repeated practice in the cognitive domain. Their results suggest that exposure to a computer placebo condition, interaction with a clinician and non-specific cognitive challenges also produce non-specific improvements in neurocognitive function (Kurtz et al., 2007). On the other hand, when general stimulation placebo conditions were compared to process-specific rehabilitation approaches other studies had found discrete improvements (Fisher et al., 2010; Vinogradov et al., 2009).

Regarding computerized CR intervention exposure time, the average time was approximately 2.93 h per week, and the average of total intervention time was 59.10 h. Only one RCT tested different exposure time with the same intervention (Fisher et al.,

Table 2
Study groups and interventions design.

ID	Study groups	Intervention	Approach	Modality	Hours per week	Total (h)
1	*Neurocognitive Enhancement Therapy	C	PS	m	~2.95	~59
	*Work Therapy	V	FA	m	~12.35	~247
2	*Auditory Training – 100	C	PS	i	5	100
	*Auditory Training – 50	C	PS	i	5	50
	Placebo Condition	C	GS	I	5	100
3	*Problem Solving Group	C	GS	i	~0.83	~5
	*Memory Training Group	C	PS	i	~0.83	~5
	Treatment as Usual	–	–	–	–	–
4	*Rehacop	PP	PSFA	g	~4.5	~54
	Treatment as Usual	–	–	–	~4.5	~54
5	Cognitive Behavioral Therapy	PP	FA	i	3	48
	*Cognitive Remediation Therapy	PP	GS	i	3	48
	Treatment as Usual	–	–	–	–	–
6	*Experimental Group	PP	GS	i	~0.66	~8
	Treatment as Usual	–	–	–	~0.66	~8
7	*Cognitive Remediation Therapy	C	PSGS	i	2	14
	Waiting List	–	–	–	–	–
8	*Standard Rehabilitation Treatment	PP	FA	m	~10.5	~630
	*Computer-aided Neurocognitive Remediation	C	PSGS	i	3	36
	Placebo Condition	–	–	–	3	36
9	*Immediate Treatment	C	PS	i	2	30
	Waiting List	–	–	–	–	–
10	*Cognitive Enhancement Therapy	C	GS	g	1.5	~75
	*Enriched Supportive Therapy	PP	FA	i	–	–
11	*Cognitive Remediation	C	PS	i	~2	100
	Placebo Condition	C	FA	m	~2	100
12	*Computer assisted training	C	GS	m	~2.25	~7
	*Basic Cognition Training	C	PS	m	~2.25	~7
13	*Cognitive Differentiation Program	PP	GS	g	1.5	21
	*Cognitive Differentiation Program	PP	GS	i	~0.66	~6.66
14	*Auditory Training Group	C	PS	i	5	50
	Placebo Condition	C	GS	I	5	50
15	*Integrated Psychosocial Therapy	PP	GSFA	g	1.5	~36
	Treatment as Usual	PP	FA	g	~1.5	~36
16	*Integrated Psychosocial Therapy	PP	GSFA	g	~1.5	~36
	Treatment as Usual	PP	FA	g	~1.5	~36
	*Computer-assisted cognitive remediation	C	PS	i	~1.5	~36
17	*Cognitive Remediation Therapy	PP	**GS**	i	3	40
	Treatment as Usual	–	–	–	–	–
18	*Cognitive Remediation Therapy	PP	PS	i	~3	~120
	Treatment as Usual	–	–	–	–	–
19	*Frontal Executive Program	PP	PS	i	~2.25	~27
	Activity Training Approach	PP	FA	i	~2.25	~27
	*Occupational Goal Intervention	PP	FA	i	~2.25	~27
20	*Neurocognitive Enhancement Therapy	C	PS	m	5	~130
	*Work Therapy	V	FA	m	~15	~360
21	*Computer-assisted Cognitive Remediation	C	GS	i	~2.5	36
	Placebo Condition	–	–	–	~2.5	36
22	*Cognitive Enhancement Therapy	C	GS	m	~3.38	162.27mean
	*Enriched Supportive Therapy	PP	FA	i	~0.95	45.8mean
23	*Attention Process Training	PP	PS	i	~0.71	~34.43
	Treatment as Usual	–	–	–	–	–
24	*Cognitive Rehabilitation	PP	GS	i	~0.66	~8
	Treatment as Usual	–	–	–	–	–
25	*Cognitive Remediation Therapy	PPC	PSGS	m	5	120
	Treatment as Usual	–	–	–	–	–
26	*Cognitive Remediation Training	C	PS	g	~0.75	~4.5
	*Affect Recognition Training	C	PS	g	~0.75	~4.5
	Treatment as Usual	–	–	–	–	–
27	*Neurocognitive Enhancement Therapy	C	PS	i	3.92mean	125.93mean
	*Vocational Program	V	FA	m	~6.8	~231,2
28	*Vocational Program	V	FA	m	–	–
	Waiting List	–	–	–	–	–
29	*Computer Training Remediation	C	PS	i	~5.25	~10.5
	Treatment as Usual	–	–	–	–	–
30	*Neurocognitive Enhancement Therapy	C	PS	m	~3.75	180
	*Work Therapy	V	FA	m	~15	~360

Note: C = Computer-based; PP = Paper-and-Pencil; V = Vocational; PS = Process-Specific; GS; General Stimulation; FA = Functional Adaptation; *i* = individual; g = group; m = mixed; *Rehabilitation Intervention.

2009, 2010). This trial presents two cohorts which have completed 50 h or 100 h of training, respectively, plus 6-month follow-up, (see ID 2 on Table 1 and Fig. 2) (Fisher et al., 2010). The authors' didn't find significant differences between 100 h versus 50 h intervention. However, 100 h group was the only group to achieve significantly improvements compared to placebo condition in domains such as global cognition and speed of processing (Fisher et al., 2010).

Table 3
Program's distribution.

	Computer-based (n = 21)	Paper-and-pencil (n = 16)	Combined (1)	Vocational (n = 4)
Process-specific	14	3	0	0
Individual	8	3	–	–
Group	2	–	–	–
Mixed	4	–	–	–
General stimulation	5	6	0	0
Individual	2	5	–	–
Group	1	1	–	–
Mixed	2	–	–	–
Process-specific and general stimulation	2	1	1	0
Individual	2	1	–	–
Mixed	–	–	1	
Functional adaptation	0	4	0	5
Individual	–	3	–	–
Mixed	–	1	–	5
Process-specific and functional adaptation	0	1	0	0
Group	–	1	–	–
General stimulation and functional adaptation	2	0	0	0
Group	2	–	–	–

Eight studies had examined the long-term effects of a computer-based CR intervention (see Fig. 2), but only 5 of them showed that improvements were sustained six month post-treatment (Bell et al., 2007; Fisher et al., 2010; Fiszdon et al., 2004; Hogarty et al., 2006; Poletti et al., 2010). Particularly one study showed that CR intervention effects are sustained after 2 years, not only in cognitive domains but also in social adjustment and symptoms (Hogarty et al., 2004, 2006).

One study conducted an initial 3-month randomized controlled trial and a secondary follow-up 9 months after the intervention, investigating the combined effects of computer-based enhancement and paper-and-pencil rehabilitation versus paper-and-pencil intervention alone (standard rehabilitation) (Cavallaro et al., 2009; Poletti et al., 2010). The authors found that computer-based remediation program assures sustained improvement nine months after the end of CR. Moreover, quality of life exhibited the most robust gain because it continued to increase during all assessments. These findings should be interpreted in light that all patients continued with a standard rehabilitation treatment for these 9 months.

In addition other study comparing computer condition with combined paper-and-pencil and computerized intervention showed results favoring the computer condition on cognitive measures (Vita et al., 2011b). Specifically attention rehabilitation was related to computerized intervention (Royer et al., 2012).

3.5.3. Paper-and-pencil outcomes

When paper-and-pencil programs were compared with treatment as usual (occupational therapy or maintenance of medication) it was found that paper-and-pencil programs had a greater improvement in social knowledge, social functioning, EF (Matsui et al., 2009; Penades et al., 2006; van der Gaag et al., 2002; Wykes et al., 2007a, 2007b), processing speed, verbal fluency, memory, working memory (Ojeda et al., 2012; Penades et al., 2006) and perception (van der Gaag et al., 2002). Moreover, there appears to be a significant effect of time following intervention for gains in social knowledge and EF (Matsui et al., 2009). However, one study did not find positive results favoring paper-and-pencil programs because there was a significant improvement in an unexpected direction favoring the control condition (multidisciplinary day-treatment program) (Lopez-Luengo and Vazquez, 2003). Only one study (Penades et al., 2006) compared paper-and-pencil remediation with cognitive behavioral therapy, finding significant improvements over time in the CR group on the cognitive subscale of the PANSS.

One study compared the effectiveness of two different paper-and-pencil models of intervention on EF (Frontal Executive Program [FEP] and Occupational Goal Intervention [OGI]) versus a control condition termed the Activity Training Approach (ATA) (Katz and Keren, 2011). Their results indicated that all groups improved on specifically EF measures; however, a process-specific approach benefited three cognitive measures over time, while a functional adaptation approach benefited only two different executive measures over time (Katz et al., 2011).

When controlled comparison between paper-and-pencil and computerized cognitive remediation interventions was performed, both modalities of administration showed a significantly larger effect on negative, positive and total symptom severity in comparison with usual care. However the non-computerized intervention showed a significantly better effect on processing speed and working memory variables, on which computerized intervention had smaller, trend effects; both cognitive treatments had somewhat larger effects on some functional measures, but only the computerized intervention showed a better effect on psychosocial functioning (Vita et al., 2011a, 2011b).

3.5.4. Vocational programs

Five studies used vocational programs (VOC) as an intervention. Four of them compared these programs with Neurocognitive Enhancement Therapy (NET), and one study compared VOC with a waiting list (WL) group (Bio and Gattaz, 2011). Compared with WL or VOC, the groups receiving NET + VOC or NET + WT showed significantly greater improvements on standardized scores in the WCST, the forward and backward digit span, and in the Bell Lysaker Emotion Recognition Task (BLERT) (Bell et al., 2001; Bell et al., 2007; Fiszdon et al., 2004; Greig et al., 2007). These cognitive outcomes were maintained at 6 months of follow-up, indicating long-term changes in cognition and a significant time versus group effect for NET compared with WL (Bell et al., 2007; Fiszdon et al., 2004). When comparing VOC with computer-based programs, there was no marked improvement favoring vocational interventions. However, when compared with WL, VOC had a group effect on symptoms and quality of life, and a time versus

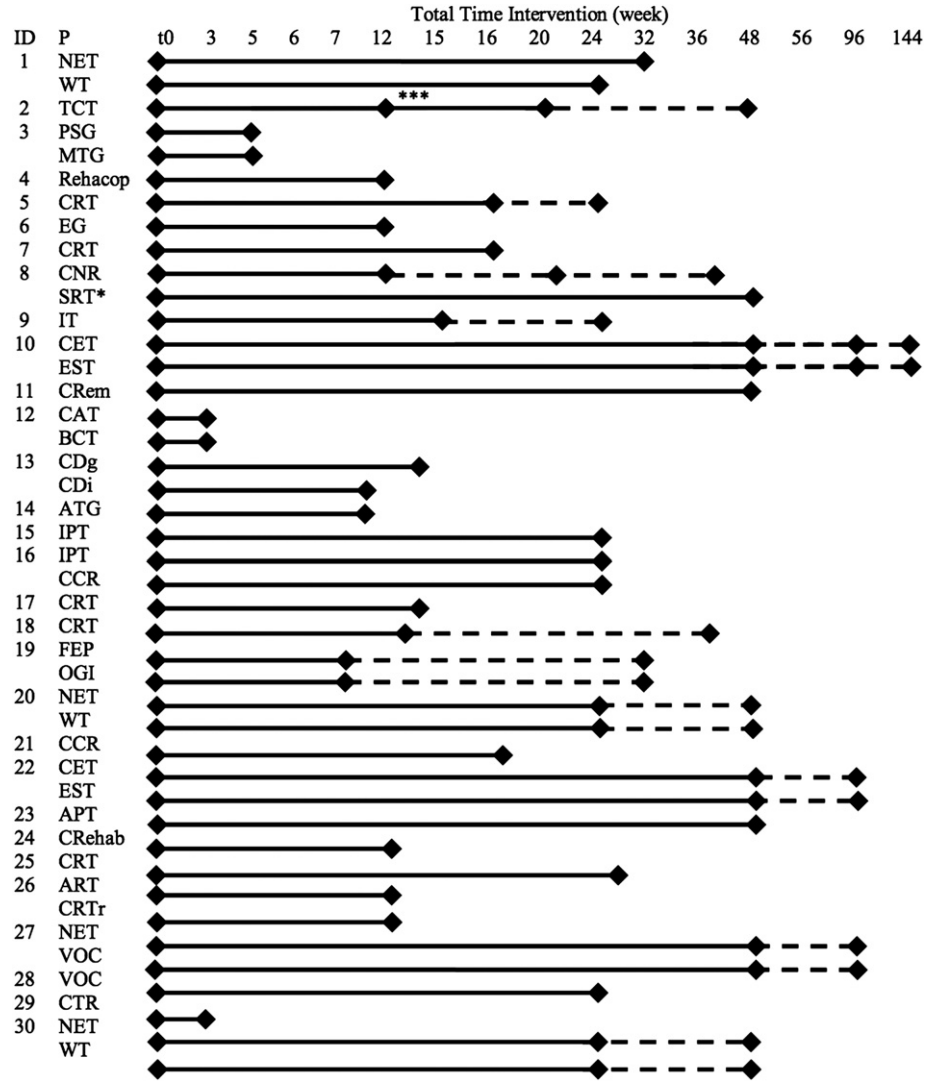

Fig. 2. *Note*: NET: Neurocognitive Enhancement Therapy; WT: Work Therapy; TCT: Target Cognitive Training; PSG: Problem Solving Group; MTG: Memory Training Group; CRT: Cognitive Remediation Therapy; EG: Experimental Group; CNR: Computer-aided Neurocognitive Remediation; IT: Immediate Treatment; CET: Cognitive Enhancement Therapy; EST: Enriched Supportive Therapy; CR: Cognitive Remediation; CAT: Computer Assisted Training; CDg: Cognitive Differentiation Program Group Condition; CDi: Cognitive Differentiation Program Individual Condition; ATG: Auditory Training Group; IPT: Integrated Psychosocial Therapy; CCR: Computer-Assisted Cognitive Remediation; FEP: Frontal Executive Program; OGI: Occupational Goal Intervention; APT: Attention Process Training; CRTr: Cognitive Remediation Training; ART: Affect Recognition Training; VOC: Vocational Program; CRT: Computer Training Remediation; t0: Baseline; P: Intervention Program; *: The intervention started 12 weeks before CNR; ***: t0 of the Auditory Training with 50 sample; ◆ Assessment; ——: Intervention Time; – – : Waiting Time.

group effect on cognitive improvements, as shown in Table 4 (Bio et al., 2011).

4. Discussion

It seems that there are a range of CR programs, each one with its own methodological characteristics and improvements specificity. Taking into account intervention issues and methodological issues, some limitations must be discussed and to be addressed in future studies. Main problems are related to the lack of standardized intervention – consequently the difficulty to replicate findings – and the poorly addressed functional and clinical outcomes – bringing limitations to the interpretability of findings. Even though, the present article corroborates the literature on the benefits of CR in schizophrenia, showing that this type of intervention could be a promising therapeutic option for individuals with executive deficits (Krabbendam and Aleman, 2003; Kurtz et al., 2001; McGurk et al., 2007b; Wykes et al., 2011).

4.1. About interventions issues

Computer-based interventions typically were favorable to vocational programs regarding cognitive domains. However, no social adjustment outcomes were even widely assessed in these studies (Bell et al., 2007; Greig et al., 2007; Fiszdon et al., 2004; Bio and Gattaz, 2011; Bell et al., 2001. Future interventions using vocational programs should include these measures because their functional adaptation approach could improve social adjustment measures. Moreover there is no clear evidence that computer-based interventions were favorable to process-specific cognitive domains, since paper-and-pencil CR significantly improved cognitive domains compared with computer-based CR (Vita et al., 2011b).

Paper-and-pencil programs compared favorably with control conditions in general. The most robust study favoring a process-specific paper-and-pencil program compared the CR with cognitive behavioral therapy (CBT) (Penades et al., 2006). The results

Table 4
Rehabilitation programs and outcomes.

ID	Programs	Sample last follow-up [age, mean (SD)]	Cognitive, clinical and social improvements
1	Neurocognitive Enhancement Therapy (NET) + Work Therapy (WT)	31 [40.3 (9.7)]	Group Effect : t1 NET + WT > t1 WT (Blert**; DS-WAIS*, WCST*) Time Effect: t1 > t0 (WCST*, DS-WAIS*, BLERT*)
	WT	34 [42.2 (7,2)]	
2	Auditory Training − 50 (AT50)	29 [42.86 (10.07)]	Time Effect: t3 > t1 (Global Cognition*; Speed Processing*; Verbal Learning*; Cognitive Control*)
	Placebo (PBO)	(a) 10 [42.9(8.06)]	
	(a) Auditory Training − 100 (AT100a)	26 [45.31 (9.39)]	Time × Group Effect: t1-t3 AT100a > t1−t3 PBOa (Verbal Learning Memory*)
	(a) Auditory Training − 50 (AT50a)	(a) 12 [48.5 (6.94)]	Time × Group Effect: t1-t3 AT100a > t1−t3 PBOa (Global Cognition*; Cognitive Control*; Speed of Processing*)
	(a) Placebo (PBOa)	(a) 10 [46.90 (9.17)]	Time × Group Effect: t1-t3 AT50a > t1-t3 PBOa (Verbal Learning*) Time × Group Effect: t0-t1 AT50 > t0-t1 PBO (Global Cognition*; Verbal Working Memory*; Verbal Learning*; Verbal Memory*)
3	Problem-solving group (PSG)	18 [36.4 (6.3)]	Group Effect : PSG > MTG + CG (ILS-PS*)
	Memory training group (MTG)	18 [33.6 (7.7)]	Time Effect: t1 PSG > t0 PSG (ILS-PS*; C-WAIS*)
	Control group (CG)	18 [39.0 (8.0)]	Time Effect: t1 CG > t0 CG (C-WAIS*)
4	Rehacop	44 [33.81(9.47)]	Time Effect: t1 > t0 (HVLT**; Stroop**; DS-WAIS*; Barcelona Verbal Fluency**; Digit Symbol MATRICS**; DAS-WHO**; PANSS**; SAI*) Time × Group Effect: Rehacop > TAU (HVLT**; Stroop*; DS-WAIS*; Barcelona Verbal Fluency*)
	Treatment as Usual	40 [37.75 (8.3)]	
5	Cognitive Remediation Therapy (CRT)	20 [34.43 (8.3)]	Group Effect: CRT > TAU (Social Functioning)
	Cognitive Behavioral Therapy (CBT)	20 [35.84 (8.5)]	Group Effect: CRT > CBT, TAU (Symptoms Cognitive Subscale*; LSP**)
	Treatment as usual (TAU)	20 [38.30 (9.1)]	Time Effect: t2, t1 in both groups > t0 in both groups on: (Working Memory**, Psychomotor Speed*, Verbal Memory**, Nonverbal memory**, Executive Function**, Social Functioning, LSP**, PANSS**) Time × Group Effect: CRT > CBT (Psychomotor Speed*, Verbal Memory*, Non-verbal memory**, Executive Function**) Group Effect : CBT > CRT, TAU (Symptoms*) Group Effect : CRT, CBT > TAU (Working Memory**)
6	Experimental Group (EG)	21 [30.4 (8.1)]	Group Effect : EG > CG (Perception*, Memory*)Time Effect: t1 > t0 (Perception**, Attention**, Memory**, Executive Functions**)
	Control Group (CG)	21 [31.7 (7.9)]	Time Effect: t1 > t0 (Attention**, Memory**)
7	Cognitive Remediation Therapy (CRT)	39 [33.4 (6.9)]	Group Effect : CRT > WL (Attention and Concentration**, Executive Functions**, Logic Thought**, Memory**)
	Waiting list (WL)	38 [32.2 (6.0)]	Time Effect: t1 > t0 (4 trained procedures: Attention and Concentration**, Executive Functions**, Logic Thought**, Memory**, Processing Speed*)
8	Computer-aided neurocognitive remediation (CNR) + Standard rehabilitation treatment (SRT)	32 [34 (9.87)]	Group Effect : t3, t2 CNR + SRT > t3, t2 SRT + PBO (Executive Function and Planning*, Psychomotor Coordination**) Time Effect: t3 > t2 > t1 > t0 (QLS*)
	Placebo (PBO) + SRT	22 [34.69 (7.63)]	Time Effect: t3 > t1 (Verbal Memory*, Working Memory**, Executive Function Planning**, Psychomotor Coordination**, QLS*) Time × Group Effect: CNR + SRT > SRT + PBO Executive Function Planning*, Psychomotor Coordination*, QLS*)
9	Immediate Treatment (IT)	–	Time Effect: t1 > t0 (RAVLT*; Rey-CFT*; CPT*; TMTB*; Social and Occupational Function Scale*) t2, t1 > t0 (RAVLT*)
	Waiting List (WL)	–	
10	Cognitive Enhancement Therapy (CET)	–	Group Effect: t1 CET > t1 EST (Processing Speed**; Neurocognition*, Social Adjustment*)
	Enriched Supportive Therapy (EST)	–	Group Effect: t2 CET > t2 EST (Processing Speed**; Neurocognition*, Social Adjustment*) Time × Group Effect: t2-t0 CET > t2-t0 EST (Processing Speed**; CVLT*; WMS*; DSS-WAIS*; GAS*) Time × Group Effect: CET > EST (Processing Speed*; Social Adjustment*)
11	Cognitive Remediation (CRem)	23 [36.7 (12.2)]	Time Effect: t1 in both groups > t0 in both groups (Working Memory**, Verbal Episodic Memory**, Spatial Episodic Memory*, Processing Speed**, Reasoning/Executive Function **) Time × Group Effect: CRem > CS (DS-WAIS*) Time Effect: t1 > t0 (DS-WAIS, A-WAIS**)
	Computer Skills (CS)	19 [32.9 (9.3)]	
12	Computer assisted training (CAT)	38 [28.03 (7.04)]	Time Effect: t1 > t0 (Plan-a-Day*, TOL*, O-AFP*, Stroop*)
	Basic Training Cognition (BCT)	39 [29.46 (7.42)]	Time × Group Effect: BCT > CAT (Stroop*)
13	Cognitive Differentiation Program (CDg)	11 [40.27 (6.6)]	Group Effect: CDg t0 > CDi t0 (BPRS*)
	Cognitive Differentiation Program (CDi)	11 [37.27(11.08)]	Time Effect: t1 CDg > t0 CDg (PA-WAIS*; A-WAIS*, BPRS*) Time Effect: t1 CDi > t0 CDi (PA-WAIS*)
14	Auditory Training Group (ATG)	25 [41.44 (11.06)]	Time × Group Effect: ATG > PC (Global Cognition*; Verbal Learning and Memory*)
	Placebo Condition (PC)	24 [46.38 (8.97)]	
15	Integrated Psychosocial Therapy − Cogpack (IPT)	16 [34.6 (7.6)]	Time × Group Effect: IPT > TAU (CVLT*; PANSS**; Self-Order Pointing Task*; Health of the Nation Outcome Scale*; Personal Social Functioning Scale*)
	Treatment as Usual (TAU)	15 [39.9 (8.6)]	Time Effect: t1 IPT > t0 IPT (Self-Order Pointing Task**; CVLT**; TMTA*; WCST*; GAF**; Health of the Nation Outcome Scale**; Personal Social Functioning Scale**) Time Effect: t1 TAU > t0 TAU (GAF*; Health of the Nation Outcome Scale*; Personal Social Functioning Scale*) Group Effect: t1 IPT > t1 TAU (Personal Social Functioning Scale*; CVLT*; Health of the Nation Outcome Scale*)
16	Integrated Psychosocial Therapy (IPT)	26 [37.15 (9.10)]	Time Effect: t1 > t0 (Processing Speed*; Working Memory*)
	Computer-assisted cognitive Remediation (CCR)	30 [36.87 (11.40)]	Time × Group Effect: IPT > TAU (Processing Speed*; Working Memory*) Time × Group Effect: CCR > IPT − Rehab (Health of the Nation Outcome Scale**)
	Treatment as Usual (TAU)	28 [43 (7.76)]	

Table 4 (*continued*)

ID	Programs	Sample last follow-up [age, mean (SD)]	Cognitive, clinical and social improvements
17	Cognitive Remediation Therapy (CRT)	21 [18.8 (2.6)]	Group Effect (WCST*)
	Treatment as Usual	19 [17.5 (2.2)]	
18	Cognitive Remediation Therapy (CRT)	43 [-(−)]	Time Effect: CRT (WCST*)
	Treatment as Usual	42 [-(−)]	Time × Group Effect: CRT > CG (WCST*; DS-WAIS*)
19	Occupational Goal Intervention (OGI)	6 [30.0 (8.8)]	Time Effect: t1 OGI > t0 OGI (Zoo Map*)
	Activity training approach (ATA)	6 [31.0 (8.3)]	Time Effect: t1 OGI > t0 OGI (EFPT*)
	Frontal Executive Program (FEP)	6 [29.0 (9.4)]	Time Effect: t1 ATA > t0 t1 ATA (EFPT*) Time Effect: t1 FEP > t0 FEP (Digit Span*) Time Effect: t1 FEP > t0 FEP (EFPT*) Time Effect: t1 FEP > t0 FEP (Zoo Map*)
20	Neurocognitive Enhancement Therapy(NET) + Work Therapy (WT)	53 [41.9(9.9)]	Time Effect t2-t1 > t0: (Executive Function*; DS − WAIS*; DSS-WAIS*; Verbal and Nonverbal Memory*; LM-WMS*)
	Work Therapy	63 [43.6 (8.1)]	
21	Computer-assisted Cognitive Remediation (CCR)	35 [46.9 (6.6)]	Group Effect: CCR > Control Group (All Rehabilitation Exercises**) Time Effect: t2, t1 CCR > t0 CCR (8 of 10 Rehabilitation Exercises*)
	Control Group	28 [48.5 (8.8)]	
22	Cognitive Enhancement Therapy (CET)	24 [25.88 (6.46)]	Group Effect: t1 CET > t1 EST (Social cognition*, cognitive style*, social adjustment**, Symptoms*)Group Effect: t2 CET > t2 EST (Social cognition*, cognitive style*, social adjustment**, Symptoms*) Group Effect: t2 CET > t2 EST Neurocognition (CVLT short term*, TMTB*, Cognitive-Perceptual and Repetition Motor Subscales*)
	Enriched Supportive Therapy (EST)	22 [25.97 (6.26)]	
23	Attention Process Training (APT)	13 [34.7 (8.4)]	Group Effect: t0 APT > t0 CG
	Control Group	11 [32.2 (8.9)]	Time Effect: t1 APT > t0 APT (WCST**) Time Effect: t1 CG > t0 CG (Dichotic Listening*)
24	Cognitive Rehabilitation (CRehab) + Treatment as usual (TAU)	11 [28.5 (6.7)]	Time Effect: t2, t1 CRehab > t0 CRehab (Script Test) Time Effect: t1 > t0 (Script Test*, RSCT*)
	TAU	9 [36.9 (7.1)]	
25	Cognitive Remediation Therapy (CRT)	28 [31 (7.6)]	Group Effect: CRT > TAU (Computerized Battery*; DS-WAIS*; Grober and Buschke*; WCST*)
	Treatment as usual (TAU)	18 [35.5 (9.0)]	
26	Affect Recognition Training (ART)	10 [31.5 (6.9)]	Group Effect: ART > CRT, TAU (Facial Affect Recognition-test*)
	Cognitive Remediation Training program (CRTr)	10 [36.7 (11.4)]	TAR > TAU (DS-WAIS*) Time Effect: t1 > t0 (Facial Affect Recognition-test**, AVLT**, DS-WAIS*)
	Treatment as Usual (TAU)	6 [35.2 (11.1)]	Group Effect: CRT > TAU (AVLT*)
27	Neurocognitive Enhancement Therapy (NET) + Vocational Program (VOC)	33 [42.53 (9.41)]	Group Effect: NET + VOC > VOC (WCST* Digit Span*)
	VOC	29 [37.69 (9.14)]	
28	Vocational Program (VOC)	47 [28.2 (7.8)]	Group Effect: VOC > WL (PANSS*, QLS*)
	Waiting list (WL)	44 [30.8 (7.0)]	Time Effect: t1 > t0 (DS-WAIS*, C-WAIS**, Stroop**, WCST*, QLS**, PANSS*) Time × Group Effect: VOC > WL (C-WAIS*, Stroop*, WCST*, PANSS*, QLS*)
29	Computer Training Remediation (CTR)	21 [32.2 (8.5)]	Group Effect: CTR > TAU (DSS-WAIS*, Word Fluency*, LM-WMS*)
	Treatment as Usual (TAU)	21 [31.6 (8.9)]	Time Effect: t1 > t0 (TMTB*)
30	Neurocognitive Enhancement Therapy (NET) + Working Therapy (WT)	45 [41.9 (9.9)]	Group Effect: t1 NET + WT > t1 WT (Digits Sequenced Recall*) Time Effect: t1 > t0 (Digits Sequenced Recall*)
	WT	49 [43.2 (8)]	Time × Group Effect: NET + WT > WT (Digits Sequenced Recall*)

Note: A-WAIS: Arithmetic, WAIS; AVLT: Auditory Verbal Learning Test; Blert: Bell Lysaker Emotion Recognition Task; BCT: Booklet Category Test; BPRS: Symptoms Brief Psychiatric Rating Scale; CVLT: California Verbal Learning Test; C-WAIS: Comprehension, WAIS; DAS-WHO: Disability Assessment Schedule; DS-WAIS: Digit Span, WAIS; DSS-WAIS: Digit Symbol Substitution, WAIS; EFPT: Executive Functions Performance Test; HVLT: Hopkins Verbal Learning Test; ILS-PS: Independent Living Scale − Problem Solving; LM-WMS: Logical Memory I and II, WMS; LSP: Life Skill Profile; MATRICS: Measurement and Treatment Research to Improve Cognition in Schizophrenia; O-AFP: Osnabruck Work Capabilities Profile; PA-WAIS: Picture Arrangement, WAIS; PANSS: Positive and Negative Syndrome Scale; QLS: Quality of Life Questionnaire; RAVLT: Rey Auditory Verbal Learning Test; RSCT: Rule Shift Cards Test; SAI: Schedule for the Assessment of Insight; Stroop: Stroop Color Word Test; TMTB: Trail Making Test B; TOL: Tower of London; WCST: Wisconsin Card Sorting Test.
t0 = Baseline t1 = Post-treatment.
t2 = Follow-up 1.
t3 = Follow-up 2.
*$p \leq 0.05$; **$p \leq 0.001$.
>positive outcome.
(a) Follow-up study with different sample.

showed that the combination of both interventions could be a standard treatment for schizophrenia. In general, process-specific paper-and-pencil programs have more positive outcomes than CBT or TAU conditions (Katz et al., 2011).

The most beneficial interventions in terms of long-term benefits were related to computer-based program (Eack et al., 2009; Fisher et al., 2009; Hogarty et al., 2006; Poletti et al., 2010) despite one study found such effect using paper-and-pencil CR presented long-term effects (Penades et al., 2006). It is very important to highlight that those studies used high frequency exposure and wide-ranging use of general stimulation approach. This could suggest that the emphasis in training should be a shift from concrete cognitive processing of information to abstraction of social themes, supporting those programs with the general stimulation developed using 2–3 h sessions per week over at least 3-month period. These data are in agreement with the neurodevelopmental epistemological basis that brain's neuroplasticity reserve can be enriched through cognitive training (Velligan et al., 2006). Taken together, this finding may indicate that the length and the intensity of the program are the key to CR intervention process. Therefore, despite speculative, considering mean frequency and duration of all CR studies that found long-term effects (IDs 2, 5, 8, 10, 30 in Table 1), suggested optimal dose would be 3 h/week for 24 weeks including process-specific and general stimulation approaches.

Another aspect about interventions issues is related to executive improvements in correspondence to real-world daily living skills

functioning. Previous findings (Reeder et al., 2006) found that where improvements in different aspects of executive functioning are present, such as schema generation or response inhibition, CR leads to improvements in social functioning regardless of baseline cognitive associations. Other authors suggest that memory changes related to CR are associated with social functioning only when they mediate the executive functioning, thus arguing that EF needs to be targeted to improve social functioning with CR in schizophrenia (Penades et al., 2010). In addition, Ritsner (2007) examined the contribution of a number of neurocognitive functions to the prediction of general and domain-specific health-related quality of life in 62 chronic schizophrenia patients, who were clinically stable and residing in the community. He found that a deficit in EF was significantly associated with impairment in general quality of life and in health-related quality of life. This is in consonance to findings that several cognitive and clinical variables significantly correlated with real-world daily living skills functioning but only the processing speed and EF emerged as independent predictors of everyday living skills scores in adolescents with early-onset schizophrenia (Puig et al., 2012). In summary, executive functioning seems to be targeted to improve social functioning with CR in schizophrenia.

4.2. About methodological issues

A previous meta-analysis (Wykes et al., 2011) found that CR benefits cannot be attributed merely to poor study methods, and, as we have also clarified, most of the programs provide real improvements in some aspect of cognitive functioning. However, the high heterogeneity of methodological procedures is a problem to the development of standardized CR programs, either in study design or in the epistemological bases of the targeted cognitive domains.

Overall, studies were not carefully blinded, and assessments were not clearly explained in the papers, given that eleven studies rated poorly (JADAD scale ≤ 2) for exactly these reasons. Other study limitations include a lack of pharmacological control since five studies did not clarify what, if any, pharmacological interventions were allowed. In general, medication effect control should be more conservative. For example, some authors found that patients with lower anticholinergic activity, who were on more conservative medication regimens, had higher ratings on positive symptoms but also showed a greater response to a computerized CR compared to patients with higher anticholinergicity (Vinogradov et al., 2009).

The long-term effectiveness of CR has not been convincingly demonstrated (Silverstein and Wilkniss, 2004) because only few studies ($n = 11$) had designed follow-up assessments (see Fig. 2) and only 06 of those had demonstrated a time per group effect (see Table 4). Taking into account that schizophrenia is a chronic psychiatric disease, CR improvements should necessarily stabilize symptoms longer than only immediately post-treatment.

Reviewed studies also demonstrated a lack of uniformity in their assessments of EF and the epistemological bases of EF theories. Such discrepancies could be observed in a long-term CR study with 44 severe mental illness participants (34 schizophrenia/schizoaffective and 10 mood disorder patients) that showed three-year stability of the benefits of CR together with an improvement in executive functioning. They found that such improvement was related to TMTB however WCST measurements were not improved by the training (McGurk et al., 2007a; McGurk et al., 2005). These problems tie together two different unresolved issues in the EF literature. On the one hand, there is a range of mutually incompatible theoretical models of EF (Baddeley, 2010; Damasio, 1996; Norman and Shallice, 1983; Stuss, 1992); and on the other hand, even with this variety, few authors explicitly commit to a theoretical framework or base their assessments on well-known models. One suggestion would be to use batteries already designed to address cognitive deficits in schizophrenia (e.g., BACS, MATRICS). As this guideline was not followed in our included studies, we considered all possible cognitive aspects in our results, understanding that a combination of measures of basic cognitive processes and functional outcomes could together illustrate complex cognitive processes, such as EF.

The present review should be interpreted considering that definitions of EF and the components and nomenclature can vary, since concepts among the different theoretical models may overlap, the same terms may be used to refer to conceptually different functions, or use different terms to refer to the same function and there is a lack of agreement among researchers on the issue of whether executive functions should be considered a single construct or a plural collection of dissociable and independent processes (Miyake et al., 2000). EF is not a single construct but an over-arching meta-construct in the service of which are various forms of self-regulation. What binds them all together as being executive in nature is that all are forms of such self-regulation. EF is quite ambiguously defined and there is little or no consensus among researchers on the precise meaning of the term. However when authors use such definition they seem to focus more on cataloging the constructs thought to be subsumed under the term and the tests believed to evaluate those constructs (Barkley, 2012). In addition, to look for keywords in the area of neuropsychological ability domains is problematic due to incomplete and subjective – and in certain cases inaccurate – indexing in the databases. Nonetheless, it is very problematic when articles are indexed with terms that are not covered by Medical Subject Headings (MeSH) Thesaurus or APA Thesaurus of Psychological Terms. However we tried to expand our search strategy including a combination of searching text words and of searching keywords that have been indexed by the databases.

The understanding of neurocognitive underpinnings of schizophrenia allows growing new treatments like CR programs. This review showed that CR could improve basic and complex cognitive domains together with daily life functioning (social abilities and work outcomes) either using computerized or paper-and-pencil programs. The findings raise many issues regarding CR clinical trials, but they are a building block to conducting future research and to help implement those treatments.

Contributors

Bruno Kluwe-Schiavon

- Wrote the first draft of the manuscript
- Managed the literature searches
- Wrote the final version of the manuscript

Breno Sanvicente-Vieira

- Wrote the first draft of the manuscript
- Managed the literature searches
- Approved the final manuscript

Christian Haag Kristensen

- Review the manuscript
- Wrote the second draft of the manuscript
- Approved the final manuscript

Rodrigo Grassi-Oliveira

- Review the manuscript
- Wrote the third draft of the manuscript
- Wrote the final version of the manuscript

Role of funding source

All authors confirm that there is no Funding Source.

Conflict of interest

Bruno Kluwe-Schiavon.
Breno Sanvicente-Vieira.
Christian Haag Kristensen,
Rodrigo Grassi-Oliveira.
All authors confirm that there are no conflicts of interest.

Acknowledgment

The authors would like to thanks CNPq for its support.

References

Baddeley A. Working memory. Current Biology 2010;20:R136–40.
Barkley RA. Executive functions: what they are, how they work, and why they evolved. New York: Guilford Press; 2012.
Bell M, Bryson G, Greig T, Corcoran C, Wexler BE. Neurocognitive enhancement therapy with work therapy – effects on neuropsychological test performance. Archives of General Psychiatry 2001;58:763–8.
Bell M, Fiszdon J, Greig T, Wexler B, Bryson G. Neurocognitive enhancement therapy with work therapy in schizophrenia: 6-month follow-up of neuropsychological performance. Journal of Rehabilitation Research and Development 2007;44:761–70.
Bell M, Tsang HWH, Greig TC, Bryson GJ. Neurocognition, social cognition, perceived social discomfort, and vocational outcomes in schizophrenia. Schizophrenia Bulletin 2009;35:738–47.
BenYishay Y. Reflections on the evolution of the therapeutic milieu concept. Neuropsychological Rehabilitation 1996;6:327–43.
Bio DS, Gattaz WF. Vocational rehabilitation improves cognition and negative symptoms in schizophrenia. Schizophrenia Research 2011;126:265–9.
Cavallaro R, Anselmetti S, Poletti S, Bechi M, Ermoli E, Cocchi F, et al. Computer-aided neurocognitive remediation as an enhancing strategy for schizophrenia rehabilitation. Psychiatry Research 2009;169:191–6.
CHMG, CHMG. How to develop a search strategy for a Cochrane Review. The Cochrane Library 2007.
d'Amato T, Bation R, Cochet A, Jalenques I, Galland F, Giraud-Baro E, et al. A randomized, controlled trial of computer-assisted cognitive remediation for schizophrenia. Schizophrenia Research 2011;125:284–90.
Damasio AR. The somatic marker hypothesis and the possible functions of the prefrontal cortex. Philosophical Transactions of the Royal Society B-Biological Sciences 1996;351:1413–20.
Dickinson D, Tenhula W, Morris S, Brown C, Peer J, Spencer K, et al. A randomized, controlled trial of computer-assisted cognitive remediation for schizophrenia. American Journal of Psychiatry 2010;167:170–80.
Eack SM, Greenwald DP, Hogarty SS, Cooley SJ, DiBarry AL, Montrose DM, et al. Cognitive enhancement therapy for early-course schizophrenia: effects of a two-year randomized controlled trial. Psychiatric Services 2009;60:1468–76.
Fisher M, Holland C, Merzenich MM, Vinogradov S. Using neuroplasticity-based auditory training to improve verbal memory in schizophrenia. The American Journal of Psychiatry 2009;166:805–11.
Fisher M, Holland C, Subramaniam K, Vinogradov S. Neuroplasticity-based cognitive training in schizophrenia: an interim report on the effects 6 months later. Schizophrenia Bulletin 2010;36:869–79.
Fiszdon JM, Bryson GJ, Wexler BE, Bell MD. Durability of cognitive remediation training in schizophrenia: performance on two memory tasks at 6-month and 12-month follow-up. Psychiatry Research 2004;125:1–7.
Goff DC, Hill M, Barch D. The treatment of cognitive impairment in schizophrenia. Pharmacology Biochemistry and Behavior 2011;99:245–53.
Greig TC, Zito W, Wexler BE, Fiszdon J, Bell MD. Improved cognitive function in schizophrenia after one year of cognitive training and vocational services. Schizophrenia Research 2007;96:156–61.
Harrison PJ. On the neuropathology of schizophrenia and its dementia – neurodevelopmental, neurodegenerative, or both. Neurodegeneration 1995;4:1–12.
Hodge MAR, Siciliano D, Withey P, Moss B, Moore G, Judd G, et al. A randomized controlled trial of cognitive remediation in schizophrenia. Schizophrenia Bulletin 2010;36:419–27.
Hogarty GE, Flesher S, Ulrich R, Carter M, Greenwald D, Pogue-Geile M, et al. Cognitive enhancement therapy for schizophrenia – effects of a 2-year randomized trial on cognition and behavior. Archives of General Psychiatry 2004;61:866–76.
Hogarty GE, Greenwald DP, Eack SM. Durability and mechanism of effects of cognitive enhancement therapy. Psychiatric Services 2006;57:1751–7.
Hutton SB, Puri BK, Duncan LJ, Robbins TW, Barnes TR, Joyce EM. Executive function in first-episode schizophrenia. Psychological Medicine 1998;28:463–73.
Jadad AR, Moore RA, Carroll D, Jenkinson C, Reynolds DJM, Gavaghan DJ, et al. Assessing the quality of reports of randomized clinical trials: is blinding necessary? Controlled Clinical Trials 1996;17:1–12.
Katz N, Keren N. Effectiveness of occupational goal intervention for clients with schizophrenia. American Journal of Occupational Therapy 2011;65:287–96.
Krabbendam L, Aleman A. Cognitive rehabilitation in schizophrenia: a quantitative analysis of controlled studies. Psychopharmacology 2003;169:376–82.
Krieger S, Lis S, Janik H, Cetin T, Gallhofer B, Meyer-Lindenberg A. Executive function and cognitive subprocesses in first-episode, drug-naive schizophrenia: an analysis of N-back performance. The American Journal of Psychiatry 2005;162:1206–8.
Kurtz MM, Moberg PJ, Gur RC, Gur RE. Approaches to cognitive remediation of neuropsychological deficits in schizophrenia: a review and meta-analysis. Neuropsychology Review 2001;11:197–210.
Kurtz MM, Seltzer JC, Shagan DS, Thime WR, Wexler BE. Computer-assisted cognitive remediation in schizophrenia: what is the active ingredient? Schizophrenia Research 2007;89:251–60.
Liu KC, Chan RC, Chan KK, Tang JY, Chiu CP, Lam MM, et al. Executive function in first-episode schizophrenia: a three-year longitudinal study of an ecologically valid test. Schizophrenia Research 2011;126:87–92.
Lopez-Luengo B, Vazquez C. Effects of Attention Process Training on cognitive functioning of schizophrenic patients. Psychiatry Research 2003;119:41–53.
Matsui M, Arai H, Yonezawa M, Sumiyoshi T, Suzuki M, Kurachi M. The effects of cognitive rehabilitation on social knowledge in patients with schizophrenia. Applied Neuropsychology 2009;16:158–64.
McGurk SR, Mueser KT, Feldman K, Wolfe R, Pascaris A. Cognitive training for supported employment: 2–3 year outcomes of a randomized controlled trial. The American Journal of Psychiatry 2007a;164:437–41.
McGurk SR, Mueser KT, Pascaris A. Cognitive training and supported employment for persons with severe mental illness: one-year results from a randomized controlled trial. Schizophrenia Bulletin 2005;31:898–909.
McGurk SR, Twamley EW, Sitzer DI, McHugo GJ, Mueser KT. A meta-analysis of cognitive remediation in schizophrenia. The American Journal of Psychiatry 2007b;164:1791–802.
Medalia A, Revheim N, Casey M. The remediation of problem-solving skills in schizophrenia. Schizophrenia Bulletin 2001;27:259–67.
Minzenberg MJ, Laird AR, Thelen S, Carter CS, Glahn DC. Meta-analysis of 41 functional neuroimaging studies of executive function in schizophrenia. Archives of General Psychiatry 2009;66(8):811–22.
Miyake A, Friedman NP, Emerson MJ, Witzki AH, Howerter A, Wager TD. The unity and diversity of executive functions and their contributions to complex "Frontal Lobe" tasks: a latent variable analysis. Cognitive Psychology 2000;41:49–100.
Norman DA, Shallice T. Attention to action – willed and automatic-control of behavior. Bulletin of the Psychonomic Society 1983;21. 354–354.
Ojeda N, Pena J, Sanchez P, Bengoetxea E, Elizagarate E, Ezcurra J, et al. Efficiency of cognitive rehabilitation with REHACOP in chronic treatment resistant Hispanic patients. Neurorehabilitation 2012;30:65–74.
Penades R, Boget T, Catalan R, Bernardo M, Gasto C, Salamero M. Cognitive mechanisms, psychosocial functioning, and neurocognitive rehabilitation in schizophrenia. Schizophrenia Research 2003;63:219–27.
Penades R, Catalan R, Puig O, Masana G, Pujol N, Navarro V, et al. Executive function needs to be targeted to improve social functioning with Cognitive Remediation Therapy (CRT) in schizophrenia. Psychiatry Research 2010;177:41–5.
Penades R, Catalan R, Salamero M, Boget T, Puig O, Guarch J, et al. Cognitive Remediation Therapy for outpatients with chronic schizophrenia: a controlled and randomized study. Schizophrenia Research 2006;87:323–31.
Poletti S, Anselmetti S, Bechi M, Ermoli E, Bosia M, Smeraldi E, et al. Computer-aided neurocognitive remediation in schizophrenia: durability of rehabilitation outcomes in a follow-up study. Neuropsychological Rehabilitation 2010;20:659–74.
Puig O, Penades R, Baeza I, Sanchez-Gistau V, De la Serna E, Fonrodona L, et al. Processing speed and executive functions predict real-world everyday living skills in adolescents with early-onset schizophrenia. European Child & Adolescent Psychiatry 2012;21:315–26.
Reeder C, Newton E, Frangou S, Wykes T. Which executive skills should we target to affect social functioning and symptom change? A study of a cognitive remediation therapy program. Schizophrenia Bulletin 2004;30:87–100.
Reeder C, Smedley N, Butt K, Bogner D, Wykes T. Cognitive predictors of social functioning improvements following cognitive remediation for schizophrenia. Schizophrenia Bulletin 2006;32(Suppl. 1):S123–31.
Ritsner MS. Predicting quality of life impairment in chronic schizophrenia from cognitive variables. Quality of Life Research: An International Journal of Quality of Life Aspects of Treatment, Care and Rehabilitation 2007;16:929–37.
Rodewald K, Rentrop M, Holt DV, Roesch-Ely D, Backenstrass M, Funke J, et al. Planning and problem-solving training for patients with schizophrenia: a randomized controlled trial. BMC Psychiatry 2011;11:73.
Royer A, Grosselin A, Bellot C, Pellet J, Billard S, Lang F, et al. Is there any impact of cognitive remediation on an ecological test in schizophrenia? Cognitive Neuropsychiatry 2012;17:19–35.
Ruiz JC, Fuentes I, Roder V, Tomás P, Dasí C, Soler MJ. Effectiveness of the cognitive differentiation program of the integrated psychological therapy group versus individual treatment. Journal of Nervous and Mental Disease DEC 2011;199(12):978–82. http://dx.doi.org/10.1097/NMD.0b013e3182392aca.

Sartory G, Zorn C, Groetzinger G, Windgassen K. Computerized cognitive remediation improves verbal learning and processing speed in schizophrenia. Schizophrenia Research 2005;75:219–23.

Schmidt SJ, Mueller DR, Roder V. Social cognition as a Mediator variable between neurocognition and functional outcome in schizophrenia: empirical review and new results by structural equation modeling. Schizophrenia Bulletin 2011;37: S41–54.

Silverstein SM, Wilkniss SM. At issue: the future of cognitive rehabilitation of schizophrenia. Schizophrenia Bulletin 2004;30:679–92.

Stuss DT. Biological and psychological-development of executive functions. Brain and Cognition 1992;20:8–23.

Twamley EW, Jeste DV, Bellack AS. A review of cognitive training in schizophrenia. Schizophrenia Bulletin 2003;29:359–82.

van der Gaag M, Kern RS, van den Bosch RJ, Liberman RP. A controlled trial of cognitive remediation in schizophrenia. Schizophrenia Bulletin 2002;28:167–76.

Velligan DI, Kern RS, Gold JM. Cognitive rehabilitation for schizophrenia and the putative role of motivation and expectancies. Schizophrenia Bulletin 2006;32: 474–85.

Vinogradov S, Fisher M, Warm H, Holland C, Kirshner MA, Pollock BG. The cognitive cost of anticholinergic burden: decreased response to cognitive training in schizophrenia. The American Journal of Psychiatry 2009;166:1055–62.

Vita A, De Peri L, Barlati S, Cacciani P, Cisima M, Deste G, et al. Psychopathologic, neuropsychological and functional outcome measures during cognitive rehabilitation in schizophrenia: a prospective controlled study in a real-world setting. European Psychiatry 2001a;26(5):276–83.

Vita A, De Peri L, Barlati S, Cacciani P, Deste G, Poli R, et al. Effectiveness of different modalities of cognitive remediation on symptomatological, neuropsychological, and functional outcome domains in schizophrenia: a prospective study in a real-world setting. Schizophrenia Research 2011b;133(1–3): 223–31.

Wölwer W, Frommann N, Halfmann S, Piaszek A, Streit M, Gaebel W. Remediation of impairments in facial affect recognition in schizophrenia: efficacy and specificity of a new training program. Schizophrenia Research Dec 15 2005; 80(2–3):295–303. http://dx.doi.org/10.1016/j.schres.2005.07.018.

Wykes T, Huddy V, Cellard C, McGurk SR, Czobor P. A meta-analysis of cognitive remediation for schizophrenia: methodology and effect sizes. The American Journal of Psychiatry 2011;168:472–85.

Wykes T, Newton E, Landau S, Rice C, Thompson N, Frangou S. Cognitive remediation therapy (CRT) for young early onset patients with schizophrenia: an exploratory randomized controlled trial. Schizophrenia Research 2007a;94(1–3):221–30.

Wykes T, Reeder C, Corner J, Williams C, Everitt B. The effects of neurocognitive remediation on executive processing in patients with schizophrenia. Schizophrenia Bulletin 1999;25:291–307.

Wykes T, Reeder C, Landau S, Everitt B, Knapp M, Patel A, et al. Cognitive remediation therapy in schizophrenia – randomised controlled trial. British Journal of Psychiatry 2007b;190:421–7.

Wykes T, Spaulding WD. Thinking about the future cognitive remediation therapy-what works and could we do better? Schizophrenia Bulletin 2011; 37:S80–90.